

Atty. Dkt. No. 0709.010.0002
United States Serial No. 10/721,091

REMARKS/ARGUMENTS

I. INTRODUCTORY REMARKS

A. RESPONSE TO RESTRICTION REQUIREMENT

In response to a restriction requirement, claims 1-18 were elected provisionally during a telephone call from the Examiner on February 1, 2005. The election of claims 1-18 is hereby affirmed.

B. SUPPORT FOR THE CLAIM AMENDMENTS AND NEW CLAIMS

Claims 1, 6, 16 and 18 have been amended; and new claims 40-58 have been added. Support for the newly presented claims and the amendments to claim 1 can be found throughout the specification and the originally presented claims. Specifically, support for the amendments to claims 1 and 6 can be found at least in paragraphs 0017, 0018, 0033 and 0073. Claim 16 has been amended to correct antecedent basis, and 18 has been amended to replace trademarked components of the claim with equivalent generic terms. New claims 40-58 have been added, and specific support for these claims can be found at least in the originally presented claims, as well as in paragraphs 0015, 0022, 0024, 0028, 0029, 0031 and 0034. Accordingly, neither the amendments to the claims nor the new claims introduces new matter to the present application. Upon entry of the amendments and the new claims, claims 1-18 and 40-58 are pending.

II. THE OFFICE ACTION OF FEBRUARY 8, 2005

A. EXAMINER'S OBJECTIONS TO THE SPECIFICATION ARE NOW MOOT

In response to the Examiner's objections to the specification, Applicants have amended the specification herein. Applicants wish to thank the Examiner for bringing typographical errors to their attention. Applicants respectfully disagree with the Examiner that the "abstract of the disclosure ... does not define that which is new in the art to which the invention pertains."

Prosecution History, U.S. Serial No. 10/721,091, Office Action dated February 8, 2005, page 4.

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Nonetheless, Applicants have amended the abstract of the disclosure solely to expedite prosecution. Accordingly, the Examiner's objections to the specification are now moot, and withdrawal of the objections to the specification is earnestly solicited.

B. THE REJECTIONS OF CLAIMS 1-18 UNDER 35 U.S.C. §112, 2ND ¶ ARE MOOT OR TRAVERSED

1. Omission of "Essential Steps"

In the Office Action dated February 8, 2005, the Examiner alleged that claim 1 was indefinite under 35 U.S.C. §112, second paragraph "as being incomplete for omitting essential steps." *Id.* Specifically, the Examiner stated that "preamble to the claim does not correspond to the method outcome." *Id.*

Applicants respectfully disagree with the Examiner's assessment that claim 1 is incomplete because the preamble does not correspond to the outcome. The preamble of the original (and current) claim stated that the method was directed towards quantifying an analyte in a sample; and the outcome of the claim indicated to one of skill in the art that measured luminescence was to be used in the quantification of the analyte. Furthermore, one of skill in the art would have read the original claim and understood that luminescence would have been generated by the labeling moiety and/or the fluorescent protein. And the Examiner is reminded that "[s]ome latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire." *MPEP*, 8th Ed. §2173.02. Nonetheless, claim 1 has been amended to better capture the commercial embodiments; and these claim amendments, although made for entirely unrelated reasons, should render moot the Examiner's rejection of claim 1 under 35 U.S.C. §112, second paragraph. Accordingly, withdrawal of this rejection is earnestly solicited.

2. "Continuously"

In the Office Action dated February 8, 2005, the Examiner alleged that claim 3 was indefinite under 35 U.S.C. §112, second paragraph, "because it is not clear what measurement

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parameter is continuous." *Prosecution History, U.S. Serial No. 10/721,091, Office Action dated February 8, 2005, page 4.* Applicants respectfully disagree that "continuous" is an indefinite parameter. Specifically, the claims, particularly when read in light of the specification, reasonably apprise one of skill in the art as to the scope of "continuous" in the context of the invention. Furthermore the specification, in paragraphs 0023 and 0078, provides explicit guidance for one of skill in the art as to the scope and utilization of the term "continuous." Accordingly, Applicants assert the claims satisfy the definiteness requirement of 35 U.S.C. §112, second paragraph. *See MPEP 8th Ed. §2173.05(a); Shatterproof Glass Corp. v. Libbey-Owens Ford Co.* 758 F.2d 613, 624 (Fed. Cir. 1985); *Georgia-Pacific Corp. v. United States Plywood Corp.* 258 F.2d 124, 136 (2d Cir. 1958)). In view of the foregoing arguments, reconsideration and withdrawal of the rejection of claim 3 as being indefiniteness is earnestly solicited.

3. "Derivatives Thereof"

In the Office Action dated February 8, 2005, the Examiner alleged that the phrase "derivatives thereof" rendered claims 10-11 indefinite under 35 U.S.C. §112, second paragraph, "because it is not clear what protein(s) are referenced or how said proteins are derivatized." *Prosecution History, U.S. Serial No. 10/721,091, Office Action dated February 8, 2005, page 4.* Applicants respectfully disagree with the Examiner's assessment that "derivatives thereof" is unclear. Specifically, one of skill in the art would read claims 10 and 11 and understand that the claims encompass functional derivatives of *any* of the recited proteins. The specification also teaches that the term derivative, when used in conjunction with periplasmic binding proteins (PBP), includes proteins that "retain at least a fraction of the binding specificity and/or affinity of the wild-type PBP." *U.S. Serial No. 10/721,091, ¶0026.* Furthermore, the specification also teaches how to prepare protein derivatives that claims 10 and 11 encompass. *See, e.g., U.S. Serial No. 10/721,091, ¶¶ 0027, 0028 and 0070.* Thus, Applicants assert that the claims, particularly when read in light of the specification, reasonably apprise those of skill in the art as to the scope of the term "derivatives thereof," when used in conjunction with PBPs. Accordingly, Applicants assert that the claims satisfy the definiteness requirement of 35 U.S.C.

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§112, second paragraph. *See MPEP 8th Ed.* §2173.05(a); *Shatterproof Glass Corp. v. Libbey-Owens Ford Co.* 758 F.2d 613, 624 (Fed. Cir. 1985); *Georgia-Pacific Corp. v. United States Plywood Corp.* 258 F.2d. 124, 136 (2d Cir. 1958)). In view of the foregoing arguments, reconsideration and withdrawal of the rejection of claims 10 and 11 as being indefiniteness is earnestly solicited.

4. “Enhanced Versions Thereof”

In the Office Action dated February 8, 2005, the Examiner alleged that the phrase “enhanced versions thereof and mutations thereof” rendered claim 13 indefinite under 35 U.S.C. §112, second paragraph “because it is not clear what protein(s) are referenced, what parameter is ‘enhanced’ or what the standard of degree of enhancement is required....” *Prosecution History, U.S. Serial No. 10/721,091, Office Action dated February 8, 2005, page 5.* Applicants respectfully disagree with the Examiner’s assessment that “enhanced” is unclear. Specifically, one of skill in the art would read claim 13 and understand that the claim encompasses enhanced versions of *any* of the recited fluorescent proteins. The specification also teaches that the term “enhanced”, when used in conjunction with fluorescent proteins, “indicates optimization of ... the proteins’ brightness or ... faster chromophore maturation.” *U.S. Serial No. 10/721,091, ¶0034.* Furthermore, the specification also teaches how to prepare the enhanced fluorescent proteins that claim 13 encompasses. *See, e.g., U.S. Serial No. 10/721,091, ¶ 0035.* Thus, Applicants assert that the claims, particularly when read in light of the specification, reasonably apprise those of skill in the art as to the scope of the term “enhanced versions thereof,” when used in conjunction with fluorescent proteins. Accordingly, Applicants assert that the claims satisfy the definiteness requirement of 35 U.S.C. §112, second paragraph. *See MPEP 8th Ed.* §2173.05(a); *Shatterproof Glass Corp. v. Libbey-Owens Ford Co.* 758 F.2d 613, 624 (Fed. Cir. 1985); *Georgia-Pacific Corp. v. United States Plywood Corp.* 258 F.2d. 124, 136 (2d Cir. 1958)). In view of the foregoing arguments, reconsideration and withdrawal of the rejection of claim 13 as being indefiniteness is earnestly solicited.

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5. "Mutations Thereof"

In the Office Action dated February 8, 2005, the Examiner alleged that the phrase "mutations thereof" rendered claim 15 indefinite under 35 U.S.C. §112, second paragraph, "because it is not clear what protein(s) are referenced." *Prosecution History, U.S. Serial No. 10/721,091, Office Action dated February 8, 2005, page 5.* Applicants respectfully disagree with the Examiner's assessment that "mutations thereof" is unclear.

Specifically, one of skill in the art would read claim 15 and understand that the claims encompass mutations of *any* of the recited fluorescent proteins. The specification also teaches that fluorescent proteins can be mutated for a variety of reasons, provided the proteins retain some degree of fluorescence. For example, the specification teaches that mutating the fluorescent proteins may result in enhanced brightness or faster maturation, or that the proteins may be mutated to prevent it from being conjugated with another entity, such as the labeling moiety. *See U.S. Serial No. 10/721,091, ¶¶0034 and 0035.* Thus, Applicants assert that the claims, particularly when read in light of the specification, reasonably apprise those of skill in the art as to the scope of the term "mutations thereof," when used in conjunction with fluorescent proteins. Accordingly, Applicants assert that the claims satisfy the definiteness requirement of 35 U.S.C. §112, second paragraph. *See MPEP 8th Ed. §2173.05(a); Shatterproof Glass Corp. v. Libbey-Owens Ford Co.* 758 F.2d 613, 624 (Fed. Cir. 1985); *Georgia-Pacific Corp. v. United States Plywood Corp.* 258 F.2d. 124, 136 (2d Cir. 1958)). In view of the foregoing arguments, reconsideration and withdrawal of the rejection of claim 15 as being indefiniteness is earnestly solicited.

6. "Lack of Antecedent Basis for DsRed2"

In the Office Action dated February 8, 2005, the Examiner alleged that "the DsRed2 mutant DsRed2(C119A)" in claim 16 lacks antecedent basis, thus rendering the claim indefinite under 35 U.S.C. §112, second paragraph. Applicants thank the Examiner for bringing this to their attention. Claim 16 has been amended to correct the lack of antecedent basis. In response

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to the Examiner's inquiry, based upon a search of the USPTO web-accessible database, "DsRed2" does not appear to be a registered trademark. Reconsideration and withdrawal of this rejection is earnestly solicited.

7. Trademarks

In the Office Action dated February 8, 2005, the Examiner alleged that "the recitation of various proprietary trademarks" renders claim 18 indefinite under 35 U.S.C. §112, second paragraph. Claim 18 has been amended to replace trademarked elements with generic names. Reconsideration and withdrawal of this rejection is earnestly solicited.

C. THE REJECTION OF CLAIMS 1-13 AND 17-18 UNDER 35 U.S.C. §102(B) IS NOW MOOT

In the Office Action dated February 8, 2005, the Examiner rejected claims 1-13 and 17-18 and alleged that these claims are anticipated by Lakowicz *et al.* (U.S. Patent No. 6,197,534). Specifically, the Examiner stated that "Lakowicz *et al.* teach a method for quantifying an analyte in a sample" *Prosecution History, U.S. Serial No. 10/721,091, Office Action dated February 8, 2005, page 5.* Without agreeing with the Examiner's assertion that Lakowicz *et al.* anticipates claims 1-13 and 17-18, claim 1 has been amended to better capture commercial embodiments, and these claim amendments now render the Examiner's rejection moot.

Specifically, claim 1 and all of its dependent claims now read on methods of detecting and quantifying levels of analytes in a sample by administering novel fusion proteins that have a weaker affinity towards their target ligands, as measured by the dissociation constant. The currently claimed methods also rely upon a resonance energy transfer between the two luminescent constituents of the fusion protein, to indicate analyte binding. Accordingly, the currently claimed invention provides (a) a novel fusion protein, as defined by the dissociation constant (K_d), and (b) the use of resonance energy transfer between luminescent constituents of the fusion protein.

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Applicants assert that Lakowicz *et al.* does not teach a method of analyte detecting using this novel combination of elements. And “[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Vertegaal Bros. v Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987) (emphasis added). Accordingly, Lakowicz *et al.* does not anticipate claims 1-13 and 17-18, as currently amended. Reconsideration and withdrawal of the Examiner’s rejection under 35U.S.C. §102(b) is earnestly solicited.

D. THE REJECTION OF CLAIMS 14-16 UNDER 35 U.S.C. §103(A) IS NOW MOOT

In the Office Action dated February 8, 2005, the Examiner rejected claims 14-16 and alleged that these claims are obvious in view of Lakowicz *et al.* (U.S. Patent No. 6,197,534) and Tsien & Campbell (U.S. Pregrant Publication No. 2003/0059835). Specifically, the Examiner stated that “it would have been obvious to one of skill in the art to modify the method of Lakowicz *et al.* with the use of DsRed2(C119A) because Tsien & Campbell discovered the importance of C119 in fluorescent protein oligomerization.” *Prosecution History, U.S. Serial No. 10/721,091, Office Action dated February 8, 2005, page 6.* Without agreeing with the Examiner’s assertion that the combination of Lakowicz *et al.* and Tsien & Campbell render claims 14-16 obvious, claim 1 has been amended to better capture commercial embodiments, and these claim amendments, incorporated by reference into claims 14-16, now render the Examiner’s rejection moot.

To establish a case of *prima facie* obviousness, the Examiner must meet three criteria. First, the Examiner must show that the references upon which she or he relied teach *every* limitation of the currently claimed invention, *In re Royka* 490 F.2d 981, 985 (C.C.P.A. 1974). Second, the Examiner must show that there is some suggestion or motivation in the references themselves, or within the knowledge of one of ordinary skill in the art, to combine the references to arrive at the claimed invention. Lastly, the Examiner must show that there is a reasonable expectation of success in combining the references, and that this expectation of success is found in the references as well. *In re Vaeck* 947 F.2d 488, 493 (Fed. Cir. 1991). Applicants assert that

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the cited art, alone or in combination, neither teach each and every limitation of the currently claimed invention, nor do the references provide any teaching, suggestion or motivation to combine the cited art to arrive at the claimed invention, with a reasonable expectation of success.

As highlighted above, Lakowicz *et al.* does not teach the combination in the currently claimed methods, and Tsien & Campbell do not rectify these deficiencies. Specifically, Tsien & Campbell teaches "variant fluorescent proteins," and does not address methods of detecting analytes in a sample. *U.S. Pregrant Publication No. 2003/0059835, ¶0004*. Furthermore, Applicants respectfully disagree with the Examiner's assertion that "Tsien & Campbell teach the use of DsRed2 ... including C119A mutant DsRed" *Prosecution History, U.S. Serial No. 10/721,091, Office Action dated February 8, 2005, page 6*. Rather, Tsien & Campbell teach a C117E mutation in an entirely different protein (DsRed), instead of a C119A mutation in DsRed2.

Likewise, Applicants respectfully disagree with the Examiner's assertion that "a particular alanine substitution ... is a matter of obvious design choice." *Prosecution History, U.S. Serial No. 10/721,091, Office Action dated February 8, 2005, page 6-7*. Indeed the Examiner's reliance upon *In re Leshin* for such an assertion is misplaced because *Leshin* holds that *known* substitutes for claimed elements *may* render a claim obvious. *Leshin* does not apply to the present case, because alanine is not a known substitute for glutamate. Indeed, a glutamate substitution (C117E) taught in Tsien & Campbell, can not possibly be deemed as a known substitute for an alanine substitution (C119A) at an entirely different position in an entirely different protein. Thus, one of skill in the art could take no guidance from Tsien & Campbell to modify Lakowicz to arrive at the claimed invention.

E. THE DOUBLE PATENTING REJECTIONS

Applicants note that the Examiner's rejections of claims 1-18 under the judicially created doctrine of obviousness-type double patenting are provisional. Therefore, Applicants will address the Examiner's arguments, upon indication of otherwise allowable subject matter. The

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Examiner is advised that the 'United States Serial No. 10/040,077, upon which the Examiner relies, has matured into U.S. Patent No. 6,855,556.

Conclusion

Claims 1, 6, 16 and 18 have been amended; and new claims 40-58 have been added. In addition, the specification, including the abstract of the disclosure has been amended to rectify the Examiner's objections thereto.

The Examiner's rejections under 35 U.S.C. §112, second paragraph are either moot in view of the claim amendments, or have been traversed. The claim amendments also render moot the Examiner's rejections of claims 1-13 and 17-18 under 35 U.S.C. §102(b). Finally, the amendments to the claims render moot the Examiner's rejection of claims 1-18 under 35 U.S.C. §103(a). Withdrawal of all outstanding rejections is earnestly solicited.

Should the Examiner believe that further discussion of any remaining issues would advance the prosecution, he or she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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